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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,770	09/10/2003	Harold A. Robertson	2817/102	6044

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,770	ROBERTSON ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *1-48 and 53-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group III, claims 49-52 in the response filed Deceember 27, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore, claims 49-52 are examined.

Informalities

The disclosure is objected to because of the following informalities:

2. Fig. 3 discloses nucleotide sequences, however, there is no sequence identifier "SEQ ID NO:" provided either in the drawing or in the brief description of the drawings. Applicants must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) and provide a paper copy and computer readable form of Sequence Listing containing "all" the sequences. Appropriate correction is required.

3. Fig. 7 contains panels A-D, however, the brief description of the drawings fails to describe each of these figures. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 49-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 49-52 are directed to a pharmaceutical formulation comprising an effective amount of a modulator of PDE10 activity in an acceptable carrier. While the specification discloses a composition comprising a compound that modulates PDE10 expression/activity can be used for treating a CAG repeat disorder such as Huntington's disease (HD), where the compound can be quinpirole, alloxan, microazole nitrate, MLD-12330A, tetracycline derivatives, (6R, 12aR)-2,3,6,7,l2,l2a-Hexahydro-6-(5-benzofuranyl)-2-methyl-pyrazino[2', 1':6,1)pyrido[3,4-b]indole-l,4-dione and its (6R, 12aR) isomers, KS-505, IC224, SCH 51866, IBMX and dipyridamole (page 4, line 17-page 5, line 5; Example 12); and the use of minocycline in the treatment of HD (Example 13), the specification does not describe the *in vitro* and *in vivo* effects of these compounds having different structures in modulating the PDE10 activity. Although the prior art (e.g., Fujishige et al., J. Biol. Chem. 274, 18438-18445, 1999; Soderling et al., PNAS 96, 7071-7076, 1999) describes the inhibition of PDE10A activity by compounds such as IBMX, dipyridamore and SCH51866 in a radiolabeled nucleotide assay, the specification provides a sequence (SEQ ID NO:12) for PDE10A from the mouse, which has only 23.6% sequence identity to homo sapiens mRNA for 3',5'-cyclic nucleotide phosphodiesterase, PED10-1 (Genbank Accession Number A8020593, June 1999; Fujishige et al., J. Biol. Chem. 274, 18438-18445, 1999; See attached sequence match). Furthermore, the specification does not describe a genus for variants of modulators of PDE10 activity in a pharmaceutical formulation comprising the modulator of PDE10 activity, nor discloses *the in vitro* or *in vivo* effects of the formulation. A single example of PDE modulator (Example 13) does not provide written

description for the genus of variants of modulators of PDE10 activity in a pharmaceutical formulation used in the treatment. The lack of description of the use and effect of the formulations comprising various modulators in the treatment of HD, and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 49-52 are indefinite as to what an effective amount of a modulator of PDE 10 activity would do? Claims 50-52 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 49-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Daugan *et al.* (U.S. Patent 5,981,527, filed on May 15, 1998) as evidenced by Robertson et al. (US 2004/0152106).

Daugan *et al.* teach an effective amount of a compound of formula (I) such as (6R, 12aR)-2,3,6,7,l2,l2a-Hexahydro-6-(5-benzofuranyl)-2-methyl-pyrazino[2', 1':6,1)pyrido[3,4-b]indole-l,4-dione as inhibitors of PDE 5 can be prepared in a suitable pharmaceutically acceptable carrier for treating various disorders such as hypertension and stroke, e.g., oral dosages of a compound of formula (I) in the range of 0.5-800 mg daily for an average adult (70 kg; corresponding to 0.007 mg/kg to 11.4 mg/kg), and the compound can be administered by oral, topical or parenteral (including intravenous, intramuscular or subcutaneous) administration (column 2, lines 1-column 3, line 55; claims 49-52). The effective amount of 6R and 12aR isomer in the composition can modulate PDE10A activity as evidenced by Robertson et al. (paragraphs [0014] and [0133]; Example 12).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loughney *et al.* (US 6,350,603, filed February 23, 1999) as evidenced by Robertson et al. (US 2004/0152106).

Loughney *et al.* disclose identification of modulators of PDE10 biological activity is used to treat disease states that arise from aberrant PDE10 activity, and modulators may be prepared in a composition with a pharmaceutically acceptable carrier for administration, where the composition is delivered in unit dose form by intravenous, intradermal or intramuscular injection or by oral, nasal or sublingual delivery, and the treatment may consist of a single dose or a plurality of doses over a period of time (column 12, line 51-column 13, line 13; Example 7) . Although the reference does not specifically indicate which compound is used in the treatment, the reference discloses some PDE10 inhibitors such as IBMX (a non-specific inhibitor; Table 1) as evidenced by Robertson et al. ([paragraph [0012]; Example 12); and specific and non-specific inhibitors of various PDE protein families have been shown to effective in treating disorders attributable, in part, to aberrant levels of cAMP or cGMP (column 2, lines 30-48). Thus, at the time of invention was made, it would have been obvious to one of ordinary skill in the art that a pharmaceutical formulation comprises an effective amount of a PDE10 inhibitor such as IBMX in the treatment of disorders attributable, in part, to aberrant levels of cAMP or cGMP (claims 49-52), which results in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
February 21, 2006